1

SEQUENCE LISTING

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<120> NOVEL KCNQ POLYPEPTIDES, MODULATORS THEREOF, AND THEIR USES IN THE TREATMENT OF MENTAL DISORDERS

<130> 794 WO

<150> US 60/391,359
<151> 2002-06-25

<160> 47

<170> PatentIn version 3.1

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gag aag aag ctg aag gtg ggc ttc gtg ggg ctg gac ccc ggc gcg ccc      96
Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly Ala Pro
            20                  25                  30

gac tcc acc cgg gac ggg gcg ctg ctg atc gcc ggc tcc gag gcc ccc     144
Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
        35                  40                  45

aag cgc ggc agc atc ctc agc aaa cct cgc gcg ggc ggc gcg ggc gcc     192
Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
    50                  55                  60

ggg aag ccc ccc aag cgc aac gcc ttc tac cgc aag ctg cag aat ttc     240
Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65                  70                  75                  80

ctc tac aac gtg ctg gag cgg ccg cgc ggc tgg gcg ttc atc tac cac     288
Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
            85                  90                  95
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gcc tac gtg ttc ctc ctg gtt ttc tcc tgc ctc gtg ctg tct gtg ttt   336
Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
          100   105   110

tcc acc atc aag gag tat gag aag agc tcg gag ggg gcc ctc tac atc   384
Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
         115   120   125

ctg gaa atc gtg act atc gtg gtg ttt ggc gtg gag tac ttc gtg cgg   432
Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
      130   135   140

atc tgg gcc gca ggc tgc tgc tgc cgg tac cgt ggc tgg agg ggg cgg   480
Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

ctc aag ttt gcc cgg aaa ccg ttc tgt gtg att gac atc atg gtg ctc   528
Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
        165   170   175

atc gcc tcc att gcg gtg ctg gcc gcc ggc tcc cag ggc aac gtc ttt   576
Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
         180   185   190

gcc aca tct gcg ctc cgg agc ctg cgc ttc ctg cag att ctg cgg atg   624
Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
        195   200   205

atc cgc atg gac cgg cgg gga ggc acc tgg aag ctg ctg ggc tct gtg   672
Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
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gtc tat gcc cac agc aag gag ctg gtc act gcc tgg tac atc ggc ttc   720
Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

ctt tgt ctc atc ctg gcc tcg ttc ctg gtg tac ttg gca gag aag ggg   768
Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
         245   250   255

gag aac gac cac ttt gac acc tac gcg gat gca ctc tgg tgg ggc ctg   816
Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
     260   265   270

atc acg ctg acc acc att ggc tac ggg gac aag tac ccc cag acc tgg   864
Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
     275   280   285

aac ggc agg ctc ctt gcg gca acc ttc acc ctc atc ggt gtc tcc ttc   912

Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
 290   295   300

ttc gcg ctg cct gca ggc atc ttg ggg tct ggg ttt gcc ctg aag gtt   960
Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305   310   315   320

cag gag cag cac agg cag aag cac ttt gag aag agg cgg aac ccg gca   1008
Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
             325   330   335

gca ggc ctg atc cag tcg gcc tgg aga ttc tac gcc acc aac ctc tcg   1056
Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
             340   345   350

cgc aca gac ctg cac tcc acg tgg cag tac tac gag cga acg gtc acc   1104
Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
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gtg ccc atg tac agt tcg caa act caa acc tac ggg gcc tcc aga ctt   1152
Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
  370   375   380

atc ccc ccg ctg aac cag ctg gag ctg ctg agg aac ctc aag agt aaa   1200
Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
385   390   395   400

tct gga ctc gct ttc agg aag gac ccc ccg ccg gag ccg tct cca agt   1248
Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
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aaa ggc agc ccg tgc aga ggg ccc ctg tgt gga tgc tgc ccc gga cgc   1296
Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro Gly Arg
             420   425   430

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Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg
             435   440   445

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Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
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ccc aag agc tgg agc ttc ggg gac cgc agc cgg gca cgc cag gct ttc   1488
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cgc atc aag ggt gcc gcg tca cgg cag aac tca gaa gaa gca agc ctc   1536
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          500   505   510

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Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
          515   520   525

acc gag gac ctg acc ccg ggc ctc aaa gtc agc atc aga gcc gtg tgt   1632
Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys
         530   535   540

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545   550   555   560

ccc tac gac gtg atg gac gtc atc gag cag tac tca gcc ggc cac ctg   1728
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Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Gln Glu Pro Arg
          580   585   590

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Leu Pro Val Gln Gln Gly Thr Arg Thr Gly Trp Ala Ser Gly Thr Lys
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ccc act gtg gcc cat ggt ggg agt gca ggg ggt gtg tgg gcg ggg cct   1872
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          610   615   620

cct ccc cac cca cgt cgg cct ctg tca gct tct gtt gtg tct tca caa   1920
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Ser Leu Phe

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Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
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Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
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Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
         115   120   125

Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
      130   135   140

Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
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Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
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Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
210   215   220

Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
               245   250   255

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               260   265   270

Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
               275   280   285

Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
               290   295   300

Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305   310   315   320

Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
               325   330   335

Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
               340   345   350

Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
               355   360   365

Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
               370   375   380

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Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser

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       435   440   445

Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
       450   455   460

Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val
   465   470   475   480

Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe
          485   490   495

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          500   505   510

Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
       515   520   525

Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys
   530   535   540

Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg
545   550   555   560

Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu
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Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Gln Glu Pro Arg
       580   585   590

Leu Pro Val Gln Gln Gly Thr Arg Thr Gly Trp Ala Ser Gly Thr Lys
       595   600   605
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Pro Thr Val Ala His Gly Gly Ser Ala Gly Gly Val Trp Ala Gly Pro
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Pro Pro His Pro Arg Arg Pro Leu Ser Ala Ser Val Val Ser Ser Gln
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Ser Leu Phe

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1   5   10   15

gag aag aag ctg aag gtg ggc ttc gtg ggg ctg gac ccc ggc gcg ccc   96
Glu Lys Lys Leu Lys Val Gly Phe Val Gly Leu Asp Pro Gly Ala Pro
            20   25   30

gac tcc acc cgg gac ggg gcg ctg ctg atc gcc ggc tcc gag gcc ccc   144
Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
        35   40   45

aag cgc ggc agc atc ctc agc aaa cct cgc gcg ggc ggc gcg ggc gcc   192
Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
    50   55   60

ggg aag ccc ccc aag cgc aac gcc ttc tac cgc aag ctg cag aat ttc   240
Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65   70   75   80

ctc tac aac gtg ctg gag cgg ccg cgc ggc tgg gcg ttc atc tac cac   288
Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
            85   90   95

gcc tac gtg ttc ctc ctg gtt ttc tcc tgc ctc gtg ctg tct gtg ttt   336
Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe

100   105   110

tcc acc atc aag gag tat gag aag agc tcg gag ggg gcc ctc tac atc   384
Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
      115   120   125

ctg gaa atc gtg act atc gtg gtg ttt ggc gtg gag tac ttc gtg cgg   432
Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
   130   135   140

atc tgg gcc gca ggc tgc tgc tgc cgg tac cgt ggc tgg agg ggg cgg   480
Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

ctc aag ttt gcc cgg aaa ccg ttc tgt gtg att gac atc atg gtg ctc   528
Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
         165   170   175

atc gcc tcc att gcg gtg ctg gcc gcc ggc tcc cag ggc aac gtc ttt   576
Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
         180   185   190

gcc aca tct gcg ctc cgg agc ctg cgc ttc ctg cag att ctg cgg atg   624
Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
         195   200   205

atc cgc atg gac cgg cgg gga ggc acc tgg aag ctg ctg ggc tct gtg   672
Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
   210   215   220

gtc tat gcc cac agc aag gag ctg gtc act gcc tgg tac atc ggc ttc   720
Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

ctt tgt ctc atc ctg gcc tcg ttc ctg gtg tac ttg gca gag aag ggg   768
Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
         245   250   255

gag aac gac cac ttt gac acc tac gcg gat gca ctc tgg tgg ggc ctg   816
Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
         260   265   270

atc acg ctg acc acc att ggc tac ggg gac aag tac ccc cag acc tgg   864
Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
         275   280   285

aac ggc agg ctc ctt gcg gca acc ttc acc ctc atc ggt gtc tcc ttc   912
Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
      290   295   300

ttc gcg ctg cct gca ggc atc ttg ggg tct ggg ttt gcc ctg aag gtt   960
Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305   310   315   320

cag gag cag cac agg cag aag cac ttt gag aag agg cgg aac ccg gca   1008
Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
               325   330   335

gca ggc ctg atc cag tcg gcc tgg aga ttc tac gcc acc aac ctc tcg   1056
Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
               340   345   350

cgc aca gac ctg cac tcc acg tgg cag tac tac gag cga acg gtc acc   1104
Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
               355   360   365

gtg ccc atg tac agt tcg caa act caa acc tac ggg gcc tcc aga ctt   1152
Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
               370   375   380

atc ccc ccg ctg aac cag ctg gag ctg ctg agg aac ctc aag agt aaa   1200
Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
385   390   395   400

tct gga ctc gct ttc agg aag gac ccc ccg ccg gag ccg tct cca agc   1248
Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
               405   410   415

cag aag gtc agt ttg aaa gat cgt gtc ttc tcc agc ccc cga ggc gtg   1296
Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg Gly Val
               420   425   430

gct gcc aag ggg aag ggg tcc ccg cag gcc cag act gtg agg cgg tca   1344
Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg Arg Ser
               435   440   445

ccc agc gcc gac cag agc ctc gag gac agc ccc agc aag gtg ccc aag   1392
Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val Pro Lys
               450   455   460

agc tgg agc ttc ggg gac cgc agc cgg gca cgc cag gct ttc cgc atc   1440
Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe Arg Ile
465   470   475   480

aag ggt gcc gcg tca cgg cag aac tca gaa gaa gca agc ctc ccc gga   1488
Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu Pro Gly
               485   490   495

gag gac att gtg gat gac aag agc tgc ccc tgc gag ttt gtg acc gag   1536
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        515              520               525

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Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg Pro Tyr
   530              535               540

gac gtg atg gac gtc atc gag cag tac tca gcc ggc cac ctg gac atg    1680
Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu Asp Met
545              550              555              560

ctg tcc cga att aag agc ctg cag tcc agg caa gag ccc cgc ctg cct    1728
Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Gln Glu Pro Arg Leu Pro
           565              570              575

gtc cag cag ggg aca aga acg ggg tgg gct tct ggg aca aag ccc act    1776
Val Gln Gln Gly Thr Arg Thr Gly Trp Ala Ser Gly Thr Lys Pro Thr
        580              585              590

gtg gcc cat ggt ggg agt gca ggg ggt gtg tgg gcg ggg cct cct ccc    1824
Val Ala His Gly Gly Ser Ala Gly Gly Val Trp Ala Gly Pro Pro Pro
        595              600              605

cac cca cgt cgg cct ctg tca gct tct gtt gtg tct tca caa agt ctg    1872
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Phe
625
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        20              25              30
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Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
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Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
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Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
              85   90   95

Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
              100   105   110

Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
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Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
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Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
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Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
      195   200   205

Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
      210   215   220

Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
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Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
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Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
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Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
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Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val Pro Lys
     450   455   460

Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe Arg Ile
465   470   475   480

Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu Pro Gly
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Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val Thr Glu
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Asp Leu Thr Pro Gly Leu Lys Val Ser Ile Arg Ala Val Cys Val Met
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Arg Phe Leu Val Ser Lys Arg Lys Phe Lys Glu Ser Leu Arg Pro Tyr
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Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu Asp Met
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Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Gln Glu Pro Arg Leu Pro
          565   570   575

Val Gln Gln Gly Thr Arg Thr Gly Trp Ala Ser Gly Thr Lys Pro Thr
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     595   600   605

His Pro Arg Arg Pro Leu Ser Ala Ser Val Val Ser Ser Gln Ser Leu
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Phe
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            20   25   30

gac tcc acc cgg gac ggg gcg ctg ctg atc gcc ggc tcc gag gcc ccc   144
Asp Ser Thr Arg Asp Gly Ala Leu Leu Ile Ala Gly Ser Glu Ala Pro
        35   40   45

aag cgc ggc agc atc ctc agc aaa cct cgc gcg ggc ggc gcg ggc gcc   192
Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
    50   55   60

ggg aag ccc ccc aag cgc aac gcc ttc tac cgc aag ctg cag aat ttc   240
Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65   70   75   80

ctc tac aac gtg ctg gag cgg ccg cgc ggc tgg gcg ttc atc tac cac   288
Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
                85   90   95

gcc tac gtg ttc ctc ctg gtt ttc tcc tgc ctc gtg ctg tct gtg ttt   336
Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
            100   105   110

tcc acc atc aag gag tat gag aag agc tcg gag ggg gcc ctc tac atc   384
Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
            115   120   125

ctg gaa atc gtg act atc gtg gtg ttt ggc gtg gag tac ttc gtg cgg   432
Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
        130   135   140

atc tgg gcc gca ggc tgc tgc tgc cgg tac cgt ggc tgg agg ggg cgg   480

Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

ctc aag ttt gcc cgg aaa ccg ttc tgt gtg att gac atc atg gtg ctc   528
Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
            165   170   175

atc gcc tcc att gcg gtg ctg gcc gcc ggc tcc cag ggc aac gtc ttt   576
Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
            180   185   190

gcc aca tct gcg ctc cgg agc ctg cgc ttc ctg cag att ctg cgg atg   624
Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
            195   200   205

atc cgc atg gac cgg cgg gga ggc acc tgg aag ctg ctg ggc tct gtg   672
Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
            210   215   220

gtc tat gcc cac agc aag gag ctg gtc act gcc tgg tac atc ggc ttc   720
Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

ctt tgt ctc atc ctg gcc tcg ttc ctg gtg tac ttg gca gag aag ggg   768
Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
            245   250   255

gag aac gac cac ttt gac acc tac gcg gat gca ctc tgg tgg ggc ctg   816
Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
            260   265   270

atc acg ctg acc acc att ggc tac ggg gac aag tac ccc cag acc tgg   864
Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
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aac ggc agg ctc ctt gcg gca acc ttc acc ctc atc ggt gtc tcc ttc   912
Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
            290   295   300

ttc gcg ctg cct gca ggc atc ttg ggg tct ggg ttt gcc ctg aag gtt   960
Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
305   310   315   320

cag gag cag cac agg cag aag cac ttt gag aag agg cgg aac ccg gca   1008
Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
            325   330   335

gca ggc ctg atc cag tcg gcc tgg aga ttc tac gcc acc aac ctc tcg   1056
Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
            340   345   350

cgc aca gac ctg cac tcc acg tgg cag tac tac gag cga acg gtc acc   1104
Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
    355   360   365

gtg ccc atg tac aga ctt atc ccc ccg ctg aac cag ctg gag ctg ctg   1152
Val Pro Met Tyr Arg Leu Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu
    370   375   380

agg aac ctc aag agt aaa tct gga ctc gct ttc agg aag gac ccc ccg   1200
Arg Asn Leu Lys Ser Lys Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro
385   390   395   400

ccg gag ccg tct cca agc cag aag gtc agt ttg aaa gat cgt gtc ttc   1248
Pro Glu Pro Ser Pro Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe
        405   410   415

tcc agc ccc cga ggc gtg gct gcc aag ggg aag ggg tcc ccg cag gcc   1296
Ser Ser Pro Arg Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala
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cag act gtg agg cgg tca ccc agc gcc gac cag agc ctc gag gac agc   1344
Gln Thr Val Arg Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser
        435   440   445

ccc agc aag gtg ccc aag agc tgg agc ttc ggg gac cgc agc cgg gca   1392
Pro Ser Lys Val Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala
    450   455   460

cgc cag gct ttc cgc atc aag ggt gcc gcg tca cgg cag aac tca gaa   1440
Arg Gln Ala Phe Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu
465   470   475   480

gaa gca agc ctc ccc gga gag gac att gtg gat gac aag agc tgc ccc   1488
Glu Ala Ser Leu Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro
        485   490   495

tgc gag ttt gtg acc gag gac ctg acc ccg ggc ctc aaa gtc agc atc   1536
Cys Glu Phe Val Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile
        500   505   510

aga gcc gtg tgt gtc atg cgg ttc ctg gtg tcc aag cgg aag ttc aag   1584
Arg Ala Val Cys Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys
        515   520   525

gag agc ctg cgg ccc tac gac gtg atg gac gtc atc gag cag tac tca   1632
Glu Ser Leu Arg Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser
    530   535   540

gcc ggc cac ctg gac atg ctg tcc cga att aag agc ctg cag tcc agg   1680

Ala Gly His Leu Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg
545   550   · 555   560

caa gag ccc cgc ctg cct gtc cag cag ggg aca aga acg ggg tgg gct   1728
Gln Glu Pro Arg Leu Pro Val Gln Gln Gly Thr Arg Thr Gly Trp Ala
        565   570   575

tct ggg aca aag ccc act gtg gcc cat ggt ggg agt gca ggg ggt gtg   1776
Ser Gly Thr Lys Pro Thr Val Ala His Gly Gly Ser Ala Gly Gly Val
        580   585   590

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Trp Ala Gly Pro Pro Pro His Pro Arg Arg Pro Leu Ser Ala Ser Val
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        35   40   45

Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
        50   55   60

Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65   70   75   80

Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
        85   90   95

Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
    100   105   110

Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
    115   120   125

Leu Glu Ile Val Thr Ile Val Val Phe Gly Val Glu Tyr Phe Val Arg
   130   135   140

Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
    165   170   175

Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
    180   185   190

Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
    195   200   205

Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
    210   215   220

Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

Leu Cys Leu Ile Leu Ala Ser Phe Leu Val Tyr Leu Ala Glu Lys Gly
    245   250   255

Glu Asn Asp His Phe Asp Thr Tyr Ala Asp Ala Leu Trp Trp Gly Leu
    260   265   270

Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
    275   280   285

Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe

290   295   300

Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
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Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
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Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
          340   345   350

Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
          355   360   365

Val Pro Met Tyr Arg Leu Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu
          370   375   380

Arg Asn Leu Lys Ser Lys Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro
385   390   395   400

Pro Glu Pro Ser Pro Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe
          405   410   415

Ser Ser Pro Arg Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala
          420   425   430

Gln Thr Val Arg Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser
          435   440   445

Pro Ser Lys Val Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala
          450   455   460

Arg Gln Ala Phe Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu
465   470   475   480

Glu Ala Ser Leu Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro
          485   490   495

Cys Glu Phe Val Thr Glu Asp Leu Thr Pro Gly Leu Lys Val Ser Ile
          500   505   510

Arg Ala Val Cys Val Met Arg Phe Leu Val Ser Lys Arg Lys Phe Lys
          515   520   525

Glu Ser Leu Arg Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser
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Ala Gly His Leu Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg
545   550   555   560

Gln Glu Pro Arg Leu Pro Val Gln Gln Gly Thr Arg Thr Gly Trp Ala
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Ser Gly Thr Lys Pro Thr Val Ala His Gly Gly Ser Ala Gly Gly Val
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     35   40   45

Lys Arg Gly Ser Ile Leu Ser Lys Pro Arg Ala Gly Gly Ala Gly Ala
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Gly Lys Pro Pro Lys Arg Asn Ala Phe Tyr Arg Lys Leu Gln Asn Phe
65   70   75   80

Leu Tyr Asn Val Leu Glu Arg Pro Arg Gly Trp Ala Phe Ile Tyr His
      85   90   95

Ala Tyr Val Phe Leu Leu Val Phe Ser Cys Leu Val Leu Ser Val Phe
     100   105   110

Ser Thr Ile Lys Glu Tyr Glu Lys Ser Ser Glu Gly Ala Leu Tyr Ile
   115   120   125

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Ile Trp Ala Ala Gly Cys Cys Cys Arg Tyr Arg Gly Trp Arg Gly Arg
145   150   155   160

Leu Lys Phe Ala Arg Lys Pro Phe Cys Val Ile Asp Ile Met Val Leu
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Ile Ala Ser Ile Ala Val Leu Ala Ala Gly Ser Gln Gly Asn Val Phe
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Ala Thr Ser Ala Leu Arg Ser Leu Arg Phe Leu Gln Ile Leu Arg Met
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Ile Arg Met Asp Arg Arg Gly Gly Thr Trp Lys Leu Leu Gly Ser Val
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Val Tyr Ala His Ser Lys Glu Leu Val Thr Ala Trp Tyr Ile Gly Phe
225   230   235   240

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Ile Thr Leu Thr Thr Ile Gly Tyr Gly Asp Lys Tyr Pro Gln Thr Trp
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Asn Gly Arg Leu Leu Ala Ala Thr Phe Thr Leu Ile Gly Val Ser Phe
     290   295   300

Phe Ala Leu Pro Ala Gly Ile Leu Gly Ser Gly Phe Ala Leu Lys Val
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Gln Glu Gln His Arg Gln Lys His Phe Glu Lys Arg Arg Asn Pro Ala
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Ala Gly Leu Ile Gln Ser Ala Trp Arg Phe Tyr Ala Thr Asn Leu Ser
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Arg Thr Asp Leu His Ser Thr Trp Gln Tyr Tyr Glu Arg Thr Val Thr
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Val Pro Met Tyr Ser Ser Gln Thr Gln Thr Tyr Gly Ala Ser Arg Leu
     370   375   380

Ile Pro Pro Leu Asn Gln Leu Glu Leu Leu Arg Asn Leu Lys Ser Lys
385   390   395   400

Ser Gly Leu Ala Phe Arg Lys Asp Pro Pro Pro Glu Pro Ser Pro Ser
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Lys Gly Ser Pro Cys Arg Gly Pro Leu Cys Gly Cys Cys Pro Gly Arg
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Ser Ser Gln Lys Val Ser Leu Lys Asp Arg Val Phe Ser Ser Pro Arg
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Gly Val Ala Ala Lys Gly Lys Gly Ser Pro Gln Ala Gln Thr Val Arg
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Arg Ser Pro Ser Ala Asp Gln Ser Leu Glu Asp Ser Pro Ser Lys Val
465   470   475   480

Pro Lys Ser Trp Ser Phe Gly Asp Arg Ser Arg Ala Arg Gln Ala Phe
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Arg Ile Lys Gly Ala Ala Ser Arg Gln Asn Ser Glu Glu Ala Ser Leu
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Pro Gly Glu Asp Ile Val Asp Asp Lys Ser Cys Pro Cys Glu Phe Val
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545   550   555   560

Pro Tyr Asp Val Met Asp Val Ile Glu Gln Tyr Ser Ala Gly His Leu
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Asp Met Leu Ser Arg Ile Lys Ser Leu Gln Ser Arg Val Asp Gln Ile
     580   585   590

Val Gly Arg Gly Pro Ala Ile Thr Asp Lys Asp Arg Thr Lys Gly Pro
    595   600   605

Ala Glu Ala Glu Leu Pro Glu Asp Pro Ser Met Met Gly Arg Leu Gly
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Lys Val Glu Lys Gln Val Leu Ser Met Glu Lys Lys Leu Asp Phe Leu
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Val Asn Ile Tyr Met Gln Arg Met Gly Ile Pro Pro Thr Glu Thr Glu
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Ala Tyr Phe Gly Ala Lys Glu Pro Glu Pro Ala Pro Pro Tyr His Ser
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Pro Glu Asp Ser Arg Glu His Val Asp Arg His Gly Cys Ile Val Lys
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Ile Val Arg Ser Ser Ser Ser Thr Gly Gln Lys Asn Phe Ser Ala Pro
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Pro Ala Ala Pro Pro Val Gln Cys Pro Pro Ser Thr Ser Trp Gln Pro
     705   710   715   720

Gln Ser His Pro Arg Gln Gly His Gly Thr Ser Pro Val Gly Asp His
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Gly Ser Leu Val Arg Ile Pro Pro Pro Pro Ala His Glu Arg Ser Leu
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Glu Asp Thr Pro Gly Cys Arg Pro Pro Glu Gly Asn Leu Arg Asp Ser
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Asp Thr Ser Ile Ser Ile Pro Ser Val Asp His Glu Glu Leu Glu Arg
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Ser Phe Ser Gly Phe Ser Ile Ser Gln Ser Lys Glu Asn Leu Asp Ala
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Leu Asn Ser Cys Tyr Ala Ala Val Ala Pro Cys Ala Lys Val Arg Pro
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Tyr Ile Ala Glu Gly Glu Ser Asp Thr Asp Ser Asp Leu Cys Thr Pro
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Gly Lys Arg Arg Arg Asp Asp Ile Ser Val Asp Ser Leu Asp Phe Thr
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Lys Lys Ile Leu His Thr Ala Trp His Pro Ala Glu Asn Ile Ile Ala
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Leu Cys Asp Lys His Ser Lys Leu Phe Glu Glu Pro Glu Asp Pro Ser
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Phe Ser His Ser Asp Arg Tyr Met Leu Thr Arg Asp Tyr Leu Thr Val
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Lys Val Trp Asp Leu Asn Met Glu Ala Arg Pro Ile Glu Thr Tyr Gln
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Val His Asp Tyr Leu Arg Ser Lys Leu Cys Ser Leu Tyr Glu Asn Asp
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Cys Ile Phe Asp Lys Phe Glu Cys Ala Trp Asn Gly Ser Asp Ser Val
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Ile Met Thr Gly Ala Tyr Asn Asn Phe Phe Arg Met Phe Asp Arg Asn
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Thr Lys Arg Asp Val Thr Leu Glu Ala Ser Arg Glu Ser Ser Lys Pro
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Arg Asp Asp Ile Ser Val Asp Ser Leu Asp Phe Thr Lys Lys Ile Leu
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